PATENT
Docket No. **29556.1540 (SU-1976) (Formerly 176/63170)**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Goldman et al.	Examiner: R. Hutson
Serial No.	:	09/282,239	Art Unit: 1652
Cnfrm. No.	:	8339	
Filed	:	March 31, 1999	
For	:	A METHOD FOR ISOLATING AND PURIFYING OLIGODENDROCYTES AND OLIGODENDROCYTE PROGENITOR CELLS	

REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. § 41.41, appellants hereby submit their reply brief in response to the Examiner's Answer, mailed on April 11, 2011 ("Examiner's Answer"). There are no fees due at this time since this reply brief is being filed within two (2) months from date of mailing. However, the Office is hereby authorized to charge/credit Account No. 50-5409 for any deficiency/overage.

I. STATUS OF CLAIMS

A. Claims 25, 26, and 29-44 Are Finally Rejected

Claims 42-44 have been finally rejected under 35 U.S.C. § 112, as failing to comply with the written description requirement.

Claims 25, 26, and 29-41 have been finally rejected. The Examiner's Answer, dated April 11, 2011, states that these claims are rejected under 35 U.S.C. § 102(e) as being anticipated by, or under 35 U.S.C. § 103(a), for obviousness over U.S. Patent No. 6,361,996 B1 to Rao et al. ("the '996 Patent") as evidenced by Scherer et al., *Neuron* 12:1363-75 (1994) ("Scherer").

B. Claims 1-24, 27-28, and 45 Have Been Canceled

Claims 1-24, 27-28, and 45 have been canceled.

C. No Claims Stand Allowed

No claims stand allowed.

D. Claims 25, 26, and 29-44 Have Been Appealed

The decision of the examiner finally rejecting claims 25, 26, and 29-44 has been appealed.

II. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

(1) Rejection of claims 42-44 as failing to comply with the written description requirement of the first paragraph of 35 U.S.C. § 112.

(2) Rejection of claims 25, 26, and 29-41, under 35 U.S.C. § 102(e), as being anticipated by or, under 35 U.S.C. § 103(a), for obviousness over the '996 Patent as evidenced by Scherer.

III. ARGUMENT

This Reply Brief is in response to the new points of argument raised in the Examiner's Answer. Appellants maintain the arguments made in the Appeal Brief.

A. The '996 Patent Does Not Anticipate or Render Obvious the Claimed Invention

1. The Scherer Reference

On page 5 of the Examiner's Answer, the Examiner states that claims 25, 26, and 29-41 are rejected under 35 U.S.C. § 102(e), as being anticipated by, or, under 35 U.S.C. § 103(a), for obviousness over the '996 Patent as evidenced by Scherer. The Examiner did not use Scherer as a reference in the statement of rejection in the previous Final Office Action. However, it is mentioned on p. 4 of the final rejection. Therefore, this statement of the rejection under 35 U.S.C. § 102(e) and 35 U.S.C. § 103(a) as anticipated by or obvious over the '996 Patent as evidenced by Scherer may constitute a new ground of rejection. With regard to the reliance on Scherer in the outstanding office action, appellants have the following comments.

Scherer discloses that two major isoforms of 2'3'-cyclic nucleotide phosphodiesterase ("CNP"), 48 and 46 kDa, are produced from a single gene by alternative splicing. In addition, messenger mRNA encoding the larger isoform is transcribed from a separate promoter, approximately 1 kb upstream from that encoding the smaller isoform. Scherer further discloses that those two CNP isoforms are differentially expressed during the process of oligodendrocyte maturation. Scherer discloses that in oligodendrocyte precursors, only the mRNA encoding the larger protein is found, but that at the time of oligodendrocyte differentiation, both CNP mRNAs are induced. Therefore, according to Scherer, these patterns of CNP expression are likely due to stage-specific transcriptional regulation of the two CNP promoters during the process of oligodendrocyte differentiation.

Nothing in Scherer overcomes the deficiencies of the '996 Patent as set forth in appellants' Appeal Brief, as noted *infra*.

2. The '996 Patent

Appellants' maintain the arguments with regard to the '996 Patent which are set forth in their Appeal Brief. The following comments are submitted in response to new points raised in the Examiner's Answer.

It is asserted on pages 7-9 of the Examiner's Answer that Example 7 at column 13, lines 17-26 of the '996 Patent identifies the claimed invention. This is completely incorrect. All that this passage says is that there are cells which have a different morphology than that customarily present in oligodendrocytes or the multipotential oligodendrocyte-type 2-astrocyte (O2A) progenitors with an astrocytic bias (i.e. cells 14 and 54 in Figures 1 and 2, respectively, of the '996 Patent). However, there is no indication in the '996 Patent that the cells with this unique morphology have the properties of the claimed cells. To the contrary, the GalC immunoreactivity of the flattened cells in Example 7 of the '996 Patent demonstrates that they are simply oligodendrocytes. Indeed, the '996 Patent states that GalC is a marker "characteristic of oligodendrocytes" (see column 13, lines 24-26). Similarly, the present application refers to galactocerebroside which is GalC (see Figure 7F and its description on page 8, lines 28-30) as a marker for oligodendroctyes which mature from oligodenderocyte progenitor cells. See page 8, lines 28-30 and page 21, lines 24-28 of the present application. Similarly, Figure 4 of the present application identifies mature oligodendrocytes as GalC positive while the oligodendrocyte progenitors whose differentiation produces the oligodendrocytes does not have the GalC positive designation. It is the ability of appellants' oligodendrocyte progenitor cells "to further develop into galactocerebroside positive oligodendrocytes" (as opposed to already being galactocerebroside positive oligodendrocytes) that is explicitly set forth in the pending claims. Since GalC is a marker for oligodendrocytes, the flattened cells in Example 7 of the '996 Patent cannot be the claimed cells and, therefore, Example 7 of the '996 Patent cannot support the rejection based on this reference.

The Examiner's Answer makes much of calling the flattened cells intermediate between the oligodendrocytes and the multipotential oligodendrocyte-type 2-astrocyte (O2A) progenitors of '996 Patent. To the extent that argument is made with the intention of suggesting that these flattened cells are less differentiated than oligodendrocytes, nothing could be further from accurate. The GalC positive marker associated with these cells makes clear that they are oligodendroctyes.

Even if one were to overlook the GalC positive character of the flattened cells, there is no evidence that the flattened cells bear other characteristics of appellants' cells as set forth in the claims. In particular, the claims call for appellants' cells to be "human mitotic oligodendrocyte progenitor cells." The cells in Example 7 of the '996 Patent are clearly not human, and there is no evidence whatsoever that they are mitotic. Indeed, the mitotic

character of the claimed oligodendrocyte progenitor cells is an important aspect of how they are distinguishable from oligodendroctyes.

Page 14 of the Examiners' Answer asserts that the multipotential neuroepithelial stem cells and lineage-restricted astrocyte/oligodendrocyte precursor cells (cell type 14 in Figure 2) are encompassed by the oligodendrocyte progenitor cell limitation of the claims. Appellants respectfully disagree. In making this argument, what the Examiner's Answer overlooks is that claims do not simply call for an oligodendrocyte progenitor cell, but for oligodendrocyte progenitor cells where "the majority of cells in the enriched or purified preparation [of human oligodendrocyte progenitor cells] differentiate into O4 positive oligodendrocytes." As noted in the Appeal Brief, the cells of the '996 Patent cannot meet this limitation, because the multipotential neuroepithelial stem cells and lineage-restricted astrocyte/oligodendrocyte precursor cells of the '996 Patent have an astrocytic bias.

Perhaps, the most troubling aspect of the Examiner's Answer is the statement on page 16 that "**contrary to the declaration of Dr. Rao**, there is evidence of such a cell type" (i.e. a progenitor that differentiates exclusively into an oligodendrocyte). That evidence is said to be "found in Example 7 of the ['996 Patent]." However, as noted above, Example 7 does not teach what the examiner wants it to teach. Worse yet, the examiner's position seems to be that he can adhere to his own unsupported beliefs and disregard what Dr. Rao has to say in spite of the fact that Dr. Rao has expertise in the field and clearly is in a far best position to evaluate his own research results and come to a conclusion of what they demonstrate. There is no indication that the examiner has expertise in Dr. Rao's field of research nor is there any evidence that the examiner has himself observed Dr. Rao's research first hand. Under these circumstances, the examiner's decision to disregard Dr. Rao's declaration testimony is entirely improper and should not be countenanced by the Board of Patent Appeals and Interferences.

On pages 7-8 of the Examiner's Answer, it is argued that motivation to use the methods of Rao to isolate an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells in humans to treat neurological disorders in humans is provided by the '996 Patent which successfully isolates an enriched or purified preparation of mitotic oligodendrocyte progenitor cells from rat. For all of the reasons noted above, the '996 Patent does not produce such cells and on that basis alone cannot support an obviousness rejection. Nowhere in the Examiner's Answer is it explained why those skilled in the art would be interested in making human counterparts of the flattened oligodendrocytes of the '996 Patent (as opposed to the claimed human oligodendrocyte progenitor cells).

There is clearly no mention of such flattened cells other than in Example 7 of the '996 Patent, and the description of those cells in that example is so oblique that those of skill in the art would have had no reason to consider them anything special, let alone had a desire to try to produce them.

3. Conclusion

For all the reasons set forth herein and in appellants' Appeal Brief, the rejections of the claims should be reversed.

Respectfully submitted,

Date: June 13, 2011

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